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DISEASES OF THE NERVOUS SYSTEM

A PRACTICAL JOURNAL ON PSYCHIATRY AND NEUROLOGY

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DISEASES of the NERVOUS SYSTEM

(PUBLISHED MONTHLY)

A PRACTICAL JOURNAL ON PSYCHIATRY AND NEUROLOGY

EDITORIAL COMMENT

Psychiatric Therapeusis in General Practice

Justifiable criticism has been leveled at teachers of psychiatry because they fail to give the student or physician specific methods for treating nervous disorders. The senior student often sums up his course of psychiatric instruction with the statement that he has been taught how to evaluate and diagnose nervous disorders but practically nothing about the handling of these patients. This is not a local failing; rather there seems to be a universal tendency on the part of teachers to ignore the fundamentals and concentrate on the scientific or more unusual aspects of a condition in question. The beginner must be shown exactly how to apply the therapeutic measures, and in the field of psychiatry, there is some negligence in this respect.

The average physician is neither interested in nor equipped to manage the psychotic patient and will send this group of patients to a psychiatric hospital. The doctor is complaining because he was not provided with the means of treating the milder nervous conditions which are so common in general practice. This journal along with other medical journals, both psychiatric and otherwise, has published many articles on the psychoneuroses, the mild depressions, and the inadequate personalities. Such literature is excellent, first because it provides the stimulus to look for and diagnose the functional illnesses. In the second place, the mechanism for production of the illness is explained which calls attention to the fact that the seat of the trouble is most often in the emotional life of the individual. Also various psychotherapeutic techniques are outlined, and a few special methods of treatment which are applicable to certain categories are described, such as the insulin, metrazol, and electroshocks and even pre-frontal lobotomies. In the past these methods have been used only by the specialist in mental and nervous diseases. Psychotherapy in itself is always necessary, and unless a formal type, each physician works out an individual routine. While their general use cannot be recommended, certainly some shock therapy can be utilized by physicians outside of the dominion of psychiatry. This is well illustrated by a young internist who was seeking information about electro-shock therapy as he had the usual number of mild depressive reactions in his practice. In a section remote from psychiatric facilities many of these patients were unable to consult a psychiatrist, thus making it necessary to have some procedure which would be more effective for interrupting the illness than the routine of encouragement and suggestive therapy. Electro-shock has given the best results in these cases, and the cost of the apparatus is within reason. This type of shock has many advantages over metrazol, such as the patient's willingness to accept treatment, but the drug is always available to anyone interested in its use. The application of shock therapy in depressions by this internist is a good example of the many practical psychiatric procedures that are available to the physician.

(Continued to page 329)

The Treatment of Trigeminal Tic Douloureux

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Dr. Echols was graduated from the University of Michigan Medical School in 1931 and received his postgraduate training at the University of Michigan Hospital. In 1937 he was Assistant Professor of Surgery and in charge of Neurosurgery at Tulane University of Louisiana School of Medicine. He is a member of the American College of Surgeons, the American Academy of Neurological Surgery, and a diplomate of the American Board of Neurological Surgery.

Probably no person ever suffers more acutely than one experiencing a severe attack of trigeminal tic douloureux. One of its harrowing features is the sudden way in which the pain strikes—like a bolt of lightning. One of its few comforting features is the abruptness with which the paroxysm terminates. Between the first stab of pain and the last, a matter of seconds or minutes, the victim is in agony. Fortunately, a group of seizures is usually followed by a remission of weeks or months. However, spontaneous permanent relief is unknown and the patient is more or less on a continuous pilgrimage in search of salvation from pain.

Tic douloureux is believed by some to have been familiar to such illustrious medical men as Hippocrates, Aretaeus, Galen and Avicenna, but the earliest recorded case of the disease is found in the second volume of the publications of the Imperial Leopoldiniam Academy of Natural Sciences in 1671.[1] Not only is there a portrait of the victim, Dr. Johannes Laurentius Bausch, undergoing an attack, but an accurate description of the disease is given. In 1756, Nikolaus André[2] bestowed the term "tic douloureux" on this condition. In 1776 appeared the classic description of Fothergill,[3] whose name is still associated with the disease. However, it was not until 1821 that Bell[4] in England and Magendie[5] in France first recognized that the fifth rather than the seventh cranial nerve supplies sensation to the face. With this discovery, progress in therapy began. The names of Hartley, Krause, Rose, Frazier, Spiller, Cushing, Dandy and Sjoqvist each represent a stepping stone in the development of the surgical treatment of the disease.

Unceasing efforts to determine the cause of this pain have not yet succeeded. No constant pathologic changes have been demonstrated. Innumerable theories have been propounded, but no acceptable explanation has yet been offered. Among the multitude of possible etiologic factors, allergy, trauma, syphilis, disseminated sclerosis, functional neurosis, dental caries and infected paranasal sinuses have been considered, only to be discarded as inadequate. Leriche,[6] among others, believes that the pain originates in the gasserian ganglion. Harris[7] suggests as the primary cause a septic terminal neuritis in the nerve filaments in the jaw. Dandy[8] explains certain cases by pressure of arterial loops on the sensory root of the nerve. Some writers[9] attribute the syndrome to a degenerative lesion of the nucleus. Fay[10] suggests that the pain may originate in the degenerated nerves of deciduous teeth. The diversity of opinion concerning the pathogenesis of the disease emphasizes its obscurity.

Trigeminal neuralgia affects but a small proportion of the general population. Spurling[11] estimates that it represents about 5 per cent of neurologic complaints. The disease usually begins between the ages of 40 and 60, but has been reported in younger persons. The right side of the face is involved slightly more often than the left; both sides are affected in approximately 3 per cent of cases. When only one branch of the nerve is affected, the third, second and first divisions are involved in that order of frequency. The disease may spread from one division to another so that the pain is felt in the distribution of two or all three branches. In only about 15 per cent of the cases does the pain involve the entire half of the face.

No warning aura precedes an attack of trigeminal neuralgia. The seizure strikes with an excruciating, lancinating pain in one side of the cheek, lip or gum, lasting a few seconds. However, the paroxysms may occur so close together that the patient is led to believe that the attack lasts many minutes. Rarely does an attack actually last as long as fifteen minutes. As abruptly as the pain appears, it vanishes. Following an attack there may be a transient aching, numbness or hyperesthesia of the face. Chewing, rubb-

ing the face, pinching the cheeks and closing the eyes tightly are only a few of the methods to which the victim resorts in an effort to diminish the intolerable pain. So vivid is the impression of the first attack in the patient's mind that he can usually relate many years later every incident associated with its occurrence. Between attacks the patient is perfectly well.

Most persons with tic douloureux have a small area on the cheek, at the angle of the mouth, on the lip or at the side of the nose which precipitates an attack when touched. Stimulation of this region (called the "trigger zone") by talking, chewing or even a slight breeze may initiate an attack. During remissions the trigger zone disappears. The patient may attribute remissions to medication or extraction of teeth. As the disease progresses, the intervals between attacks become shorter and the intensity of the pain increases. If the condition is unilateral, pain never crosses the midline. In bilateral tic douloureux, attacks on both sides are practically never experienced simultaneously.

Since there are no sensory changes nor other objective findings in this condition, the diagnosis depends almost exclusively upon the history. A few patients are willing to demonstrate an attack by stimulating the trigger zone. Remission produced by alcohol injection of the involved division of the fifth nerve is only occasionally necessary for verification of the diagnosis.

The pain of tic douloureux must be differentiated from pain caused by diseased teeth and sinuses, which is a dull ache with gradual onset and slow disappearance. Among other conditions to be considered in the differential diagnosis are various headaches, pain caused by tumors and cysts of the face and jaw, herpes zoster, and inflammatory diseases, aneurysms or tumors near the gasserian ganglion.

Although persistent investigation has failed to penetrate the veil which beclouds our knowledge of the cause of trigeminal neuralgia, efforts directed toward alleviating the pain have been productive. Almost as long as the disease has been known, various medications including iodides, calcium gluconate, ergotamine tartrate, arsphenamine, quinine, aconite, strychnine, gelsemium, antipyrin, phenacetin, cannabis indica, nitroglycerin, pilocarpin, castor oil, atropin, salicylates and prostigmin have been advocated only to be abandoned as ineffective. Probably no pharmaceutic preparation has escaped a fair trial. Analgesics and narcotics have been used with little success, because the paroxysms are too short to give these agents time to act. For the same reason, few victims are morphine addicts. However, in spite of these discouraging experiences with drugs, medication to alleviate the symptoms is justified when the attacks are mild and the intervals long.

The drug which has been most effective in reducing the severity and number of attacks of tic douloureux (but not in curing it) is trichlorethylene. It was introduced in 1915 by Plessner[12] at the suggestion of Oppenheim. The usual dosage is 15 drops on a handkerchief to be inhaled three or four times a day over a period of three or four weeks. It is then withheld for a similar period. It can be obtained inexpensively in a one ounce bottle. Glaser[13] found that 15 per cent of a collected series of cases receiving trichlorethylene therapy were completely relieved of symptoms. However, there is no specific reference as to follow-up study on his cases. It is generally agreed that these inhalations merely bring about alleviation or remission.

More recently, various vitamin preparations, particularly vitamin B_1, have been tried. The rationale of this therapy is based on the supposition that this disease, like certain neuritides, is the result of vitamin deficiency. Opinion as to adequate dosage varies. Borsook et al.[14] report the treatment of 58 patients with tic douloureux by means of large doses of vitamin B_1. They recommend daily injections of 10 mg. of thiamine chloride. It may be given intravenously or intramuscularly. This is supplemented in refractory cases by liver extract (15 V. S. P. anti-anemia units per cubic centimeter) in 0.5 cc. doses given intramuscularly thrice weekly. If relief is not obtained after several months, the daily dose of thiamine chloride is increased to 100 mg. Of the 58 patients, 37 are classified as definitely improved, 15 improved, 3 slightly improved and 3 unimproved. These patients were under observation from six to fourteen months.

Other reports on vitamin B_1 therapy are concerned with isolated cases, although Baksh[15] reports 7 cases, with beneficial re-

sults in 6. It is obviously too early to evaluate the role of vitamins in the treatment of tic douloureux. Cure of the disease or satisfactory control over a period of years has yet to be reported. On the other hand, patients who fail to obtain lasting benefit from vitamin therapy are being seen daily, collectively speaking, at the neurosurgical clinics.

Some writers have reported success with such diverse therapies as hyperpyrexia, local diathermy or short wave therapy, cold quartz lamp, roentgen and radium irradiation, massage, electrolysis, cauterization and galvanism. That these agents have not been generally adopted is indicative of their inefficacy.

Surgical destruction of the trigeminal nerve pathways is the only therapy which produces instant relief from attacks of tic douloureux. The supraorbital, infraorbital, mental or alveolar branches of the nerve may be injected with 50 to 95 per cent alcohol in quantities ranging from one-fourth to one cubic centimeter. The resulting anesthesia and relief from pain may last for many months, but regeneration of the nerve and recurrence of the pain is inevitable. Avulsion of the supraorbital or infraorbital nerves is usually practiced only after injection has proved inadequate. Even avulsion of these branches is followed by regeneration of the nerves and return of pain.

Alcohol injection of the maxillary and mandibular divisions of the nerve is extensively practiced. This requires more skill and study than injection of the smaller branches. A longer needle is needed and one to five cubic centimeters of alcohol is injected. The assistance of a textbook and a skull is essential for those making such injections infrequently. Relief of pain is sometimes obtained for as long as eighteen months after a successful injection. Injection of the ophthalmic division of the nerve is dangerous and rarely attempted.

The chief objections to alcohol infiltration of one of the main divisions of the nerve are the transient relief obtained and the painfulness of the procedure. It must be performed under local anesthesia, as only by producing pain can the operator know that he has reached the nerve. Directing the needle toward the mandibular division at the foramen ovale, the operator inserts it just below the notch in the inferior surface of the zygomatic ridge and slowly pushes it medially until it reaches a depth of 4 to 4.5 cm. The maxillary division is injected at its point of emergence from the skull through the foramen rotundum. The needle is introduced beneath the anterior end of the zygoma, just anterior to the coronoid process. Pushing it posteriorly, medially and upward to a depth of about 5 cm., the operator encounters the nerve.

Repeated treatments become increasingly less effective because of scar formation, but patients whose pain is neither frequent nor severe enough to persuade them to accept operation should enjoy the temporary benefits of injection of the peripheral nerves. This form of therapy is also indicated in the more severe cases if the patient is physically unfit to undergo the operation.

Of all the nonoperative procedures for the relief of trigeminal neuralgia, alcohol injection of the gasserian ganglion is the most effective. Unfortunately, it is also the most difficult, most uncertain and most dangerous of procedures for the treatment of the disease. This is not the most desirable therapy for tic douloureux because it is extremely painful; it is unsuccessful about half of the time even with experienced operators; it can precipitate multiple cranial nerve palsies; and the pain frequently returns because of survival of some of the ganglion cells. The needle is inserted through the cheek just below the anterior end of the zygoma and directed toward the foramen ovale. Novocaine is injected into the mandibular division to permit passage of the needle through the foramen ovale into the body of the ganglion without excessive pain. Two precautions should be taken. The needle should be aspirated with a syringe to make certain that the point is not free in the subarachnoid space and the alcohol should be injected not faster than one drop a minute.

Intracranial section of the fifth nerve is the treatment advocated in all neurosurgical clinics. It may be accomplished either through the temporal or cerebellar routes. The temporal approach is preferred by most surgeons, although it is the more technically difficult. The object of the procedure is to section some or all of the sensory root of the nerve, depending on the distribution of pain, without disturbing the motor root which supplies the

muscles of mastication. If the pain is limited to the distribution of the maxillary and mandibular divisions, the fibers supplying the cornea and forehead are left intact. Because the roots are sectioned central to the cell bodies of the gasserian ganglion, regeneration cannot take place and the resulting anesthesia and relief from pain is permanent.

Many unjustified rumors concerning the unfavorable effects of operation (and alcohol injection) are still current. There is some basis for these. One and sometimes two deaths may occur in each 100 cases. These are usually caused from apoplexy. Actually, the mortality is extremely low in view of the fact that about 20 per cent of the patients are past the age of 65. The motor root of the trigeminal nerve is occasionally damaged, resulting in some difficulty in mastication and in a perceptible atrophy of the masseter and temporal muscles on one side. Since the chewing muscles of the opposite side still function, the patient has no more than a minor handicap. The muscles supplied by the seventh nerve occasionally become paralyzed (Bell's palsey) several hours or days following operation. Complete recovery eventually takes place except in rare instances. The incidence of the complication of temporary Bell's palsey is about 2 per cent. Keratitis, corneal ulceration and even loss of the eye are occasionally seen. If tic douloureux involves the optic region, the entire sensory root must be sectioned at operation. This leaves the cornea anesthetic and diminishes lacrimation. Subsequently, because of carelessness or even in spite of care, changes in the eye occur. The wearing of glasses, daily washing of dust from the eye and proper treatment of minor infections will usually prevent ophthalmic complications. Approximately 10 per cent of patients complain after operation of numbness of the face. The patient may also be aware of crawling sensations and other paresthesias in the anesthetic area. This is, from the surgeon's point of view, the most serious complication of the operation. No entirely satisfactory remedy is known. Many patients complain of minor discomforts such as the tendency of food to become "lost" in the anesthetic half of the mouth. However, this is soon overcome and the complaint is never heard after the first few months.

There are both advantages and disadvantages of the medical, injection and surgical treatments. Patients who avoid surgical intervention never can be certain that they are cured. They must try one drug after another and submit to repeated alcohol injections. Those accepting operative treatment know that the pain cannot return. All surgical patients are restored to full activity. There is practically no instance in recent years of a patient who regretted having had surgical section of the trigeminal nerve for tic douloureux. An incomplete survey shows that over 2,000 patients are operated on each year in this country.

It would be a definite advancement in the surgical therapy of this disease if the pain sense could be abolished without disturbing the sense of touch. Recently, Sjoqvist[16] reported the achievement of this end by sectioning the bulbo-spinal root of the fifth cranial nerve by making an appropriate incision in the medulla oblongata. He was able to stop the pain of trigeminal neuralgia and at the same time to preserve touch sensation in 20 cases. Others[17,18,19] have reported similar results. Subjective numbness and post-operative paresthesia are thus abolished. In spite of the abolition of the corneal reflex in every instance, no visual complications developed. That cases have been reported in which the tongue or lip was not rendered insensitive to painful stimulation calls attention to possible uncertainty of results following this operation. The complications which would result from injury to the restiform body, nucleus of Burdach, spino-thalamic tract and recurrent laryngeal fibers of the vagus must be considered in evaluating such a procedure. It is still too early to speculate as to the possibilities of the operation of Sjoqvist in the treatment of trigeminal tic douloureux.

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Mental Hygiene and the Defense Program

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To be mentally healthy an individual must have made an adequate adjustment with his community group, local, national, and international, which satisfies his personal requirements and provides security within the social structure.

To live, to be alive, is a dynamic function. There is continuous change in ideas and institutions. We may oppose these changes, perhaps by reason of fear of the unknown consequences, but we also may welcome these very changes when through the democratic process they are discussed freely, studied and then tested. Our confidence in this procedure is based on the knowledge that, whatever of the change proves unsatisfactory, can be modified by us.

Of late we have been confronted by the dynamics of the totalitarian regime. Here, also, there is continuous change in ideas and institutions. But the changes are imposed from above by the few who determine of themselves what is to be the method of living, irrespective of the desires of those affected. Opposition is destroyed without consideration of its value.

The present war is part of this same ruthless technique. Those resisting must be totally eradicated; they have declared themselves in opposition to the totalitarian philosophy.

In any democracy there is discontent with the failures and inadequacies of the social structure. The individuals and social groups involved are critical and resentful. The totalitarian rulers utilize these discontents to produce disintegration within the nation and by economic pressure and terror-propaganda methods cause disruption between civil authority and citizen, and between group and group.

We see throughout the world, in response to the above assaults, the collapse of our altruistic, aesthetic and ethical ideals. We see science debased in the service of destruction.

To counteract these forces will require great moral strength, and a gathering together of our faith and confidence in our way of living. It will require the development through our military, naval and air forces, of such strength that we will feel secure in our nation. It will require the development of a sound basic

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solidarity and morale in our community and industrial relations. At present, we must reassess our strength and our weakness. In terms of mental hygiene for the community this means a study of our interpersonal relationships in three fields:

1) The civilian population that will not be utilized in active defense, but which must support the defending forces.

2) The defense forces themselves.

3) The families of the individuals called to defense service.

The first group is of much greater importance in the present type of warfare than it has been since primitive tribal wars. Defending forces, because of the complexities of mechanized warfare, are wholly dependent on the capacity of the mobilized industrial, transport and food producing capacity of the civilian population.

Because of this great dependence, the defense forces are highly sensitive to the state of morale behind the lines. For defense forces to know that civilian morale is split, broken or disintegrating under the influence of subversive ideas, is to reduce their capacity to hold out in a crisis.

It is essential then to study those types of individuals that are susceptible to propaganda designed to break unity. They are the people who have either failed to adjust themselves in ordinary life or who, making a superficial adjustment, are protected by a routine habitual environment which is now being broken up. Such individuals, latently insecure, seem to respond, either by adopting the suggestions of alien propaganda, or by succumbing to panic which may infect others.

This acceptance of ideas is not necessarily made on an intellectual basis, but rather on the individual's basic emotional attitude. There is the over-suggestible, over-credulous, emotionally unstable type who tends to respond to whatever is the most recently promulgated idea without criticism or judgment —"to hear is to act." There is also the suspicious, over-sensitive type who finds the cause of his failures in the fancied persecution of himself by others, such as his employer, his social group, or his "luck." This group, because of actual or implied promise of redress of their imagined wrongs, may adopt in full faith the alien subversive ideas and become the fanatical advocates of the "new order."

One other large group exists. This is the group with active or latent criminal tendencies. They are susceptible to alien inducements due to their anti-social trends and because of their own cupidity. Through destruction and disintegration of the existing law-abiding social structure, they expect to secure rich returns in position and possessions.

Few of the above active groups seem to realize that as soon as they have served their purpose they too will be eliminated if the enemy is successful.

Then we have the large mass of our people. They have passively accepted the concept that their social structure exists, but they make little effort to determine why it exists or what they must do to keep it so.

They have also been overwhelmed through our present means of mass communication by floods of information, misinformation and contradictory report. They tend to resent this and end by disbelieving everything. Such an attitude is dangerous from the point of view of mental hygiene. It must be the function of all interested in mental health to work for correction of this attitude. Also, from a mental hygiene point of view, an uncritical over-enthusiasm for any one group of ideas, be they ever so right, contains just as many dangerous implications for that individual as a constant disbelief and pessimism.

We may further expect that with the increasing demands for service, both in industry and in the defense forces, many individuals with latent inadequacies will develop difficulties under the increasing stress. A proportion of these can be stabilized by psychiatric treatment. Others may be supported by mental hygiene given through workers with an understanding of the underlying emotional problems. Still others will show detrimental symptoms and require rejection. This will increase the load of psychiatric cases.

According to Pollock[10] there was such an increase in 1917-1918. He states: "Following the entrance of the United States into the war, a marked increase occurred in new admissions to hospitals for mental disease. This was especially noticeable in the alcoholic, manic-depressive and dementia praecox groups. The rate of new cases in the alcoholic group was nearly fifty per cent higher in

1917 than in 1916. The rise in rates in other groups was significant although less striking. As the war continued, the excitement died down. The populace, instead of standing back and deploring conditions, became united in the effort to win the war. The national morale was raised; crime and drunkenness were notably reduced and the rate of incidence of mental disease decreased. The dreaded insecurity did not come during the war period nor during the following decade."

Reports from both civilian and military British clinics[5,6,7] indicate the occurrence of neuroses similar to those occurring in the last war. However, they are not occurring on as large a scale as anticipated. The reports[6] indicate, among civilian groups, two types of setting for the reaction. The first occurred in anticipation of actual assaults on Britain and among the more highly educated, intellectual and responsible section of the population. There was a variety of reactions, but mainly of the reactive depressions. The second setting was in relation to actual bombing. Each case suffered bombing and had some degree of involvement of consciousness, but over 50 per cent of the group had had previous neurotic upsets or were recognized as neurotic in their adjustment. The reaction tended to be one of amnesia with some hysterical manifestation. Over 50 per cent of the cases responded to psychiatric treatment within three days and recovered. The others required longer hospital treatment.

Another interesting observation was the relation noted between mental reactions and diet.[4] The British dietary council has been reinforcing the diet with Vitamin A, calcium and Vitamin B_1. Their observations have shown that with a reduction of Vitamin B_1 the following reactions were observed: moodiness, sluggishness, indifference, fear and excessive fatigue. This state is serious for a civilian group under tension, either for sustained industrial effort, or for calm and careful consideration of ideas designed to create emotional disturbances. An almost normal intake, on the other hand, maintained individuals in apparently good health, and when the intake was raised to 600 international units per day, alertness increased and capacity for work doubled.

Every factor having to do with our physical and mental well-being must be available to the population as a whole.

Registrants

Under the present system of examining registrants, every effort is made to eliminate those cases that have mental liabilities which would prevent their adjustment under the increased stress of military training. The mentally defective, the epileptic, the neurotic, the alcoholic, the emotionally unbalanced, as well as those of psychopathic personality, are included in this group. Needless to say those who have been psychotic or are psychotic cannot be accepted. Again, according to Pollock,[10] "Men having physical or mental diseases or defects that make them unfit for the service are rejected by draft boards. It is reported that such rejections amount to about thirty-two per cent of the men examined. The accepted men are later given examinations in camp by army surgeons and psychiatrists. These examiners find certain more or less obscure disorders and defects overlooked by draft boards. The drafted men found clearly unfit for military duty are sent home; others with minor disabilities are assigned to service best fitted for them. In 1917 and 1918, the rate of nervous and mental disorders found among the enlisted men in camps was 33 per 1000 men examined. A large part of these men had to be discharged."

The greatest difficulty will be to detect the latent maladjustments that have been successfully covered by a sheltered civilian environment, but which are quickly revealed under active military life. Many of these cases would show up if even a fair family and personal history were available. A psychiatric examination has been formulated which we hope will uncover these cases before they go to training centers. This outline appeared in the September, 1940 issue of *The Journal of Psychiatry*.[11] Other suggestions for examining physicians appeared in *Psychiatry*, November 1940.[3]

It must be appreciated that these are minimal requirements and should be used as informative guides to indicate the need for more thorough and intensive examination by the medical advisory board.

Some of this material can also be used in the instruction of line officers and non-commissioned personnel who will have intimate contact with the trainee.

The importance of instruction of medical and line personnel is noted by Baillie[12] who found that the medical examination had not included a good psychiatric check-up and that cases of maladjustment, defectiveness and epilepsy had been observed by unit commanders and non-commissioned officers, but that there had been failure to refer the case promptly for psychiatric study.

The experience in the Canadian Forces offers some suggestions for study.[2] Up to January, 1941, 1000 cases of mental maladjustment were cared for; 156 were major psychoses. In addition, of the men invalided home, 26.5 per cent had duodenal ulcer, a condition recognized as being associated with emotional tension. Baillie,[12] in a review of 200 consecutive admissions to the Neuropsychiatric service of the Christie Street Hospital, showed where an adequate examination and family and personal history would have saved in the expense of training these cases, the hospitalization and avoided the possibility of future pension cases.

He found that over 50 per cent of the cases showed bad family or environmental factors. The economic history showed 51 per cent with a bad industrial record. Fifteen per cent had a previous criminal record. Finally, direct inquiry as to previous mental disorder or difficulties was negative for 60 per cent of cases. However, in response to this direct questioning, 22 cases were found to be backward; 8 attended special school; 18 had previous psychotic disorder, 7 with admissions to mental institutions; 35 reported previous neurotic disorders requiring treatment prior to enlistment.

In discussing the question of when unsuitability should have been detected, Baillie reports: 34 per cent should have been obvious at first medical examination; 30 per cent should have been detected during the recruit training period; 2½ per cent in early military hospitalization during the preliminary training period; 13 per cent became apparent under various stresses requiring only an average degree of capacity for adjustment, such as "change of surroundings, alteration of diet, complete change of routine, separation from family (noted in the British reports) and during infection." Only 5 cases, or 2½ per cent showed service connection and none were exposed to battle conditions.

As a result of the hospital study, 20 per cent were considered at discharge as fit for general combat service, 7½ per cent for home service only, ½ per cent temporarily unfit. The remaining 72 per cent, however, were recorded as "medically unfit, emotionally unfit or not likely to make an efficient soldier under the existing standards."

The British report of one psychiatric unit[7] indicated also that many of the cases of neurotic disorder appeared under trivial stresses of army life and separation from family. It was found that the factor of constitutional weakness was of fundamental importance. These men did not seem to have the recuperative powers under stress that the well-adjusted man had.

An analysis[5] of 100 psychiatric cases of Royal Naval ratings under active service showed 43 cases of neurosis, hysteria and anxiety states, 44 of psychosis (mostly depressions), 8 psychopathic, 5 organic; 33 per cent recovered, 67 per cent were discharged as unfit. In reviewing the cases, 39 per cent were considered to be cases that could have been anticipated. Positive past personal histories were high in this group, and 11 cases had previous concussion. In the unpredictable group, positive family histories were in high proportion.

In Canada, one provincial hospital system[2] has furnished to the military examining boards a list of names of all men of military age who have had psychoses. In the United States, one state is doing this by reference through its central office, but does not furnish a list in advance.

In Canada,[2] a pool of educational and welfare agencies has been created to meet the educational, recreational, social and counselling needs of the forces. This should go far to maintaining good mental hygiene.

Our final group is composed of the families of those in the active defense forces. We are already familiar with the emotional disturbances arising in a family, consequent to a member of it becoming seriously ill, losing employment, or becoming involved in other difficulty. Similar reactions may be expected consequent to the calling up for service. Especially will this appear when there has been over-dependence or close emotional attachment to the registrant. Further, the possibility of emotional upset is increased by the

fear of the future with its unknown complications.

We must recognize that we are being subjected to the first two of the three phases of the totalitarian technique of war, namely, the economic and the propaganda. The fear that the third phase, actual assault, may develop will be an active predisposing cause of mental disturbance for susceptible family units. The importance of the family of the registrant lies in the fact that its reaction is much more intense and, therefore, has greater potentialities as a disrupting factor in the community and for the soldier or sailor.

The psychiatrist is prepared to recognize these cases and deal with them therapeutically. However, as psychiatric personnel is drawn to the armed forces, modification of therapy will have to be made. The experience in British clinics[8] under stress conditions, has shown the value of mass or group psychotherapy in reactive neuroses, or in cases of exaggeration of latent maladjustments. The technique consists of a group meeting with a psychiatrist who gives about a 20 minute talk, then sees individuals who desire more intimate advice. During this office interview period, the remainder of the group discuss the lecture among themselves. This seems to be of definite benefit, both therapeutically and also administratively, as there is psychiatric advice being made available to larger numbers with a reduced personnel.

The general practitioner, the internist, the surgeon and other specialists, may expect to find under the strain of the present situation that there is increased use of physical illness as an expression of the emotional tension either by intensification of symptoms or prolonged convalescence. The symptoms of physical illness may also be used as a means of expression of the anxiety of the patient without any demonstrable physical pathology, but with disorder of function that, if maintained long enough, would result in pathology.

The use of psychiatric consultation in such cases would be of valuable assistance to both the attending physician and the patient. In most instances, the therapy required can be best handled by the patient's own physician or surgeon as soon as recognition of the emotional factors has been ascertained. In many cases, the mere telling of the emotional problem is sufficient to discharge the tension. In others, some trained social assistance is of help. In only a few cases will it be necessary for the psychiatrist to give active therapy.

It must be the function of all physicians, social workers and welfare agencies to work to preserve the family, the registrant and the community from the ill-effects of emotional disorders. The strength and unity of the nation depend on the health of the citizens of this country.

Just as a physically healthy nation is less susceptible to infections and serious epidemics, so, a mentally healthy nation is less susceptible to the epidemics of subversive ideas and disrupting philosophies designed to destroy our faith in our social structure and our way of life.

Albany, New York.

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The Cerebrospinal Fluid Total Protein in the Psychoses

The Results of Spinal Fluid Examinations in 2,823 Mental Patients (Exclusive of the Syphilitic Psychoses)*

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In 1925 a spinal fluid laboratory was organized at the Central State Hospital of Indianapolis for the examination of the cerebrospinal fluid of neurosyphilitic patients. In the succeeding years lumbar punctures were done with increasing frequency in other psychoses. In some of these patients, including cases of dementia praecox, spinal fluid abnormalities were present which could not be explained on the basis of syphilis. At first, these fluid abnormalities were confusing, inasmuch as we thought the spinal fluid to be normal in the so-called functional or psychogenic psychoses.

A search of the literature in 1930 revealed that data on the spinal fluid of the various psychoses were practically non-existent. This encouraged us to make a systematic study, and beginning with 1931 a spinal fluid examination was done on every newly admitted patient. Later, lumbar punctures were done on all resident patients who had been admitted in the period from 1900 to 1930. By the end of 1939 the results of one or more spinal fluid examinations on every inmate of the institution were available for a statistical study.

In summarizing the outstanding findings of this serological survey, one may state that the most important spinal fluid abnormality was a slight or moderate increase of the protein content, which was present in a small number of patients of all diagnostic groups. In some instances minor changes of the colloidal gold reaction ("1", "2", and rarely "3") were noted. A cell count above 11 was observed only 5 times in these 2,823 mental patients, all of these occurring in the senile and arteriosclerotic cases.

In the following, the results of the study are given in tabulated form. Male and female patients were grouped separately, because there was a difference in the frequency of an increased protein content in the two sexes. In none of the patients was there a positive serology for syphilis in blood and spinal fluid. Cases with a positive Wassermann reaction of the blood were excluded from this report, since syphilis may produce a slightly increased protein content as the only spinal fluid abnormality.

Spinal Fluid Findings in the So-Called Psychogenic Disorders

Dementia Praecox

Number of Male Patients
(new and old cases) examined ... 642

* Presented in the form of a scientific exhibit at the ninety-sixth annual meeting of the American Psychiatric Association, Cincinnati, Ohio, May 20-24, 1940.

**Central State Hospital

With increased spinal fluid protein ... 5.0%
2 or 3 plus Pandy test; and 45 to 166 mg. of total protein.
Mean value of total protein 74 mg.

Number of Female Patients (new and old cases) examined ... 639
With increased spinal fluid protein ... 3.2%
2 or 3 plus Pandy test; and 45 to 130 mg. of total protein.
Mean value of total protein 68 mg.

Manic-Depressive Psychoses

Number of Male Patients examined 91
With increased spinal fluid protein ... 5.2%
2 plus Pandy test; and 45 to 71 mg. of total protein.
Mean value of total protein 65 mg.

No. of Female Patients examined 178
With increased spinal fluid protein ... 3.8%
2 plus Pandy test; and 45 to 92 mg. of total protein.
Mean value of total protein 60 mg.

Involutional Psychoses

Number of Male Patients examined 58
With increased spinal fluid protein ... 4.9%
2 plus Pandy test; and 45 to 71 mg. of total protein.
Not enough cases to compute accurate mean value.

No. of Female Patients examined 141
With increased spinal fluid protein ... 4.7%
2 plus Pandy test; and 45 to 91 mg. of total protein.
Mean value of total protein 60 mg.

The incidence of an increased protein content was approximately 5 per cent in the male and slightly less in the female patients in the three main groups of the psychogenic psychoses. An elevated protein content in some cases of schizophrenia has previously been reported by Kafka and Samson,[1] Plaut and Rudy,[2] Kopp,[3] Merritt and Fremont-Smith,[4] Neel,[5] Solomon, Schwab and Maletz,[6] and Bruetsch, Bahr and Skobba.[7] However, Kopp[3] examining the spinal fluid of 18 manic-depressive patients found no protein changes. The experience of Merritt and Fremont-Smith[4] with manic-depressive patients was limited to 13 cases. Their findings were within normal limits in all but 2 cases which had a protein content of 56 and 60 mg. per 100 cc. respectively.

Significance and Practical Implication of an Increased Protein Content of the Spinal Fluid in Some Cases of the Psychogenic Group

An increase in the protein content of the spinal fluid is generally considered an indication of an organic process. The question may be raised here: Are any demonstrable changes present in the central nervous system of these cases? In two dementia praecox patients with an increased protein content, necropsy observations are available. One of these cases, a 33 year old schizophrenic patient with a 3 plus Pandy test and a total protein of 130 mg., died four months after admission during a stage of catatonic excitement. Gross and microscopic examination of the brain, spinal cord and internal organs revealed nothing abnormal with present-day neuropathologic technique. In the other patient, besides a moderately thickened pia-arachnoid, equally negative findings were made on post-mortem examination. It seems, therefore, that the presence of an increased protein content of the spinal fluid does not exclude the diagnosis of dementia praecox as this condition is known today. The same statement may be made concerning the manic-depressive and involutional psychoses with an increased protein, although such cases have not yet been examined at autopsy. Furthermore, it would be of great interest to know whether or not a slight or moderate increase in the protein content may be present in some individuals of the mentally healthy general population.

Spinal Fluid Findings in the Organic Psychoses

The presence of an increased protein content in some instances of the organic psychoses is well known. In particular, patients with cerebral arteriosclerosis have been the subject of spinal fluid studies. The group of the senile psychoses, however, has never been studied systematically from the cerebrospinal fluid angle. The results of our investigations are interesting and seem to open new avenues into research on the causation of the psychoses occurring in the older age groups.

Psychoses with Cerebral Arteriosclerosis

Number of Male Patients examined 47
With increased spinal fluid protein ... 25.4%

2 or 3 plus Pandy test; and 45 to 119 mg. of total protein.

Mean value of total protein 72 mg.

No. of Female Patients examined 31

With increased spinal fluid protein ... 16.2%

2 or 3 plus Pandy test; and 45 to 104 mg. of total protein.

Mean value of total protein 72 mg.

Senile Psychoses

Number of Male Patients examined 172

With increased spinal fluid protein ... 12.7%

2 or 3 plus Pandy test; and 45 to 147 mg. of total protein.

Mean value of total protein 71 mg.

No. of Female Patients examined 130

With increased spinal fluid protein ... 2.9%

2 or 3 plus Pandy test; and 45 to 83 mg. of total protein.

Mean value of total protein 73 mg.

The highest frequency, 25.4 per cent, with an increased spinal fluid protein was found in male patients with arteriosclerotic psychoses. On the other hand, in the female patients of the same group an increased fluid protein was present in only 16.2 per cent. Even more striking differences between male and female patients were noted in the senile psychoses. In this group 12.7 per cent of the men, but only 2.9 per cent of the women had an increased amount of protein.

Post-Mortem Observations in Arteriosclerotic and Senile Psychoses with an Increased Protein Content of the Cerebrospinal Fluid

In six patients, diagnosed arteriosclerotic psychoses with an increased protein content, an autopsy was performed. In all six instances there were gross areas of cerebral softening of various size, thus explaining the spinal fluid abnormalities. A case report from this group follows:

E. A. R., a white woman, aged 74, had had a slight stroke two years previously. Following the cerebral accident she did not recognize her friends. She became hallucinated in the visual field and developed ideas of persecution.

On admission residual symptoms of the stroke were absent. The patellar reflexes were normal. The pupils reacted sluggishly to light. The blood pressure was 180/110. In the urine there was a trace of albumin and a few casts. The spinal fluid findings were as follows: Pandy: 3 plus; Ross-Jones: 1 plus; total protein: 104 mg.; cells: 8; colloidal gold reaction: 0000000000; Wassermann of spinal fluid: negative. Wassermann, Kahn and Kline of blood: negative.

At autopsy, two years later, the vessels at the base of the brain and to a lesser degree the meningeal arteries exhibited marked atherosclerosis. The meninges were clear. In the left occipital lobe was a rather large area of softening (Fig. 1). There were also several minute cystic areas of degeneration in both striate bodies and in the white matter of various regions of the brain.

If in cases of arteriosclerotic psychoses an increased amount of protein is found, one may assume that the focal areas of brain destruction are of recent date or that the lesions are progressing with the formation of new, possibly minute and symptomless areas of arteriosclerotic softenings.

In the group of the senile psychoses with an increased protein content, four cases were studied anatomically. In two instances care-

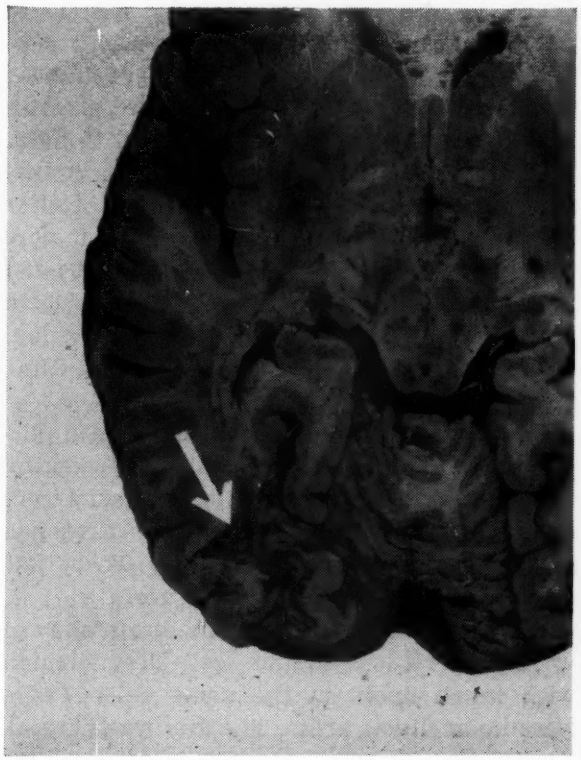

Figure 1—Arteriosclerotic softening in left occipital lobe. Spinal fluid examination revealed the following changes. Pandy: 3 plus; Ross-Jones: 1 plus; total protein: 104 mg.; cells: 8; colloidal gold reaction: 0000000000; spinal fluid Wassermann: negative. Blood Wassermann, Kahn and Kline: negative.

ful histologic examination of the brain did not reveal any manifest source of the increased spinal fluid protein. There were, however, somewhat thickened meninges. In the brain of these two patients not a single acellular area was present, i.e., areas in which the ganglion cells had completely disappeared without subsequent gliosis. The anatomic observations in these two senile psychoses resembled histologically the two cases of dementia praecox with an increased fluid protein in which microscopic examination had rendered similar negative results. In the following, a summary of one of the two cases with senile psychosis is given:

A. H. W., a white male patient, aged 74, rather suddenly became mentally unbalanced, talking incoherently and threatening those about him. He expressed delusions of persecution and was at times hallucinated. During his violent episodes several persons were needed to restrain him. In the institution he sat motionless and said nothing, unless he was spoken to. Although he gave the impression of much deterioration at the time of death, he was not untidy. If one would not consider the advanced age, the patient presented the picture of a catatonic dementia praecox. Both patellar reflexes were present. The pupils were pin-point and fixed to light. The blood pressure was 175/80. The spinal fluid changes on admission, four years after the first mental symptoms were noted, were as follows: Pandy: 2 plus; Ross-Jones: 1 plus; total protein: 83 mg.; cells: 2; colloidal gold reaction: 0011210000; Wassermann of spinal fluid: negative; Wassermann, Kahn and Kline of blood: negative.

On post-mortem examination the pia-arachnoid showed considerable thickening over the frontal-central region. The sulci were gaping. Careful dissection of the hardened brain revealed no gross pathology. There was no indication of syphilis of the aorta.

Histologic examination of the brain showed uncharacteristic ganglion cell degeneration with much lipoid in the nerve cells. There were no acellular areas. The glia was normal. Senile plaques were present in the cortex. The pia-arachnoid showed marked fibrosis.

In the two other cases of senile psychoses with an increased protein content of the spinal fluid, structural changes were found which seemed to explain the increased amount of protein. In one instance there were observed on intensive search a few microscopic cortical infarctions containing pigment-carrying scavenger cells. The meninges were moderately thickened and cloudy. In the other patient, one small, grossly visible area of cystic softening was present involving the lower cortical lamina and white matter of a frontal convolution. This area was not in communication with the subarachnoid space. There was another small infarction in the cerebellum which reached the meninges. An etiologic cause for the softenings was not determined. There was no atherosclerosis or syphilis of the brain vessels. This patient was 83 years old, when he showed the first mental symptoms. He had one son with dementia praecox in the institution, and another son with a psychosis had committed suicide before it was possible to admit him to a state hospital.

At this point it may be emphasized that normal spinal fluid findings do not exclude an organic brain lesion. On figure 2 the brain

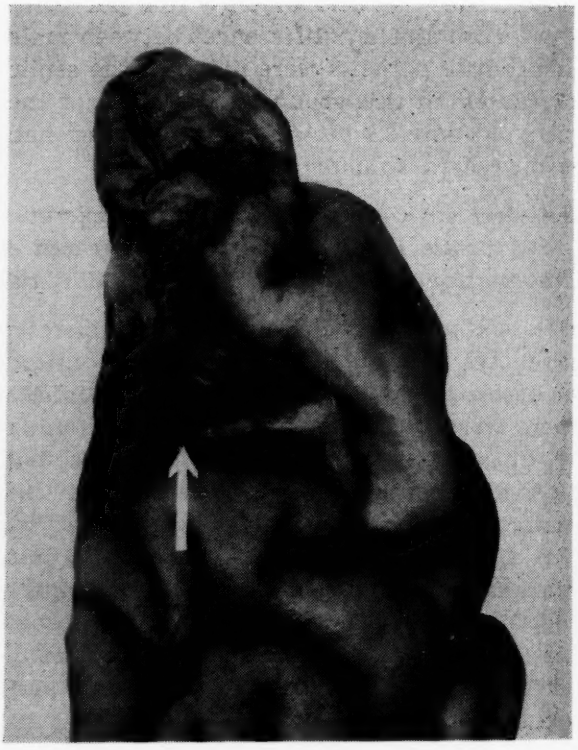

Figure 2—Normal spinal fluid findings do not exclude an organic brain lesion. The patient, aged 71, diagnosed senile psychosis, was punctured five years after admission and four weeks prior to death. The spinal fluid was entirely negative, but in frontal lobe region there was an old area of infarction.

of a patient is shown, who at the age of 71 developed mental symptoms. The diagnosis was senile psychosis. He was punctured for the first time five years after admission and four weeks prior to death. The spinal fluid was entirely normal with no increase in protein, but post-mortem examination revealed an old infraction in the frontal lobe area. In such instances much seems to depend on the time when the spinal fluid examination is made. In this case, the softening, due to rheumatic vascular disease, very likely had occurred several years previously and had set off the mental symptoms.

Psychoses with Mental Deficiency

Number of Male Patients examined 51
With increased spinal fluid protein ... 8.9%
2 or 3 plus Pandy test; and 45 to 190 mg. of total protein.
Mean value of total protein 82 mg.
No. of Female Patients examined 41
With increased spinal fluid protein ... 6.8%
2 plus Pandy test; and 45 to 67 mg. of total protein.
Mean value of total protein 65 mg.

One patient of this group was of particular significance. He was a 34 year old, well developed individual, diagnosed as psychosis with mental deficiency, moron. The patient exhibited no obvious neurologic abnormalities, and pupils and reflexes were normal. He was punctured for the first time in 1933, when spinal fluid examination revealed a 3 plus Pandy test. On repuncture in 1938 there was a 3 plus Pandy test; 2 plus Ross-Jones test; 190 mg. of total protein; 2 cells; and a colloidal gold reaction of 0012100000. In 1940 the protein had decreased to 119 mg. Spinal fluid and blood Wassermann and other tests for syphilis (Kahn and Kline) were negative on three occasions. Such outspoken spinal fluid changes in an individual who appears physically normal are difficult to understand. The question of the presence of a possible asymptomatic and incidental meningioma was raised in this patient, since we have observed practically identical spinal fluid abnormalities in a 60 year old patient with a large meningioma in the left frontal lobe area (verified by autopsy). The first spinal fluid examination in the meningioma case yielded a 3 plus Pandy test and 208 mg. of protein. Six months later the protein was 166 mg. Another spinal fluid examination was done eight months later and five months prior to death, revealing the following changes: Pandy: 3 plus; Ross-Jones: 3 plus; total protein: 125 mg.; cells: 5; colloidal gold reaction: 0011100000. The patient with mental deficiency has now been under observation for seven years with no appearance of signs of brain tumor (headaches, choked disk, etc.), and the possibility of a neoplasm can be excluded. The cause of the high protein content remains unexplained.

Spinal Fluid Findings in Other Diagnostic Groups

In other diagnostic groups the number of cases examined was not large enough to give an accurate percentage in which an increased fluid protein was present. A slight or moderate protein increase was observed in some patients who were diagnosed paranoid condition, psychoses with psychopathic personality, traumatic and epileptic psychoses. Patterson and Levi,[8] who examined a group of 50 epileptics, state that in 90 per cent of those examined for proteins the result was negative. They used for the detection of an increased protein content the Ross-Jones test only. Lennox and Merritt,[9] examining the spinal fluid of 793 epileptic patients, reported the protein content to be increased in 10 per cent.

Solomon, Schwab and Maletz[6] found spinal fluid changes in some cases of Huntington's chorea. In our material there were ten cases of Huntington's chorea. All had an entirely normal spinal fluid. Our observations are in accordance with Merritt and Fremont-Smith[4] and with Demme,[10] who also have reported normal spinal fluids in Huntington's chorea. There was, however, an additional case, first diagnosed Huntington's chorea, with a 2 plus Pandy test and a colloidal gold reaction of 0012332100. At autopsy there was no atrophy of the corpus striatum. In other words, the typical findings of Huntington's chorea were not present. On histologic examination there were noted in the cortex and in the striatum a few vessels with syphilitic endarteritis. Slight perivascular round-cell infiltrations were present about some vessels in the internal capsule, in the midbrain and in the cerebellum. Such changes are inconsistent with the pathology of Huntington's chorea.

Although the Wassermann test of the spinal fluid and of the blood was negative on repeated occasions, the histologic findings were suggestive of a rare instance of chorea on a syphilitic basis.

Another interesting observation worth mentioning was made in the group of Huntington's chorea. The daughter of a patient who had died of Huntington's chorea in another Indiana institution was admitted at the age of 31 with the diagnosis of dementia praecox. Spinal fluid examination revealed in the daughter a 2 plus Pandy test and 62 mg. of total protein. So far no symptoms of chorea have made their appearance in the daughter.

Twenty-four cases of post-encephalitic Parkinsonism were punctured. All of these had a spinal fluid protein within normal limits, and in only two instances were there slight changes ("1" and "2") in the colloidal gold curve.

Concluding Remarks

One of the more striking results of this study was the observation that the mean value of the protein content in the male schizophrenic patients was 74 mg., while the mean value in the male patients with an arteriosclerotic psychosis was only 72 mg. The mean value in the various diagnostic groups was obtained by computing the protein value of all patients who had a total protein above 45 mg.

Other observations of interest were those made in the group of Huntington's chorea and in the post-encephalitic parkinsonian patients. In both instances one is dealing with an unquestionable organic background of the mental disorder, yet the fluid protein was within normal limits.

Summary

An increased protein content has been found to be the most frequent spinal fluid abnormality in mental patients. It was observed in a varying percentage of patients of both the psychogenic and organic groups. A spinal fluid examination furnishes additional valuable information in many psychiatric patients. But this necessitates that the fluid examination be carried out as exactly as possible and by an experienced person.

Acknowledgment—Many thanks are due to Mr. Truitt C. Brown, laboratory assistant, who has been associated with our spinal fluid laboratory since its organization in 1925. His long experience in this field was of great value throughout this investigation.

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Synthetic Vitamin E in the Treatment of Amyotrophic Lateral Sclerosis and Related Disorders

Report of Six Cases

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In attempting to evaluate the effectiveness of a new drug in treating a condition commonly considered incurable, such as amyotrophic lateral sclerosis, rigid diagnostic criteria should be established. If doubt exists in the mind of the examiner concerning the precise nature of the condition under treatment, how accurately can results be interpreted with respect to the real value of the drug? Therefore, objective findings indicating involvement of the pyramidal tracts and the anterior horn cells must be clear cut in order that the condition may be placed, without question, in a certain diagnostic category. Although the condition may be suspected from the discovery of signs of pyramidal tract disease alone, one is much more certain of the ultimate clinical picture if evidence of anterior horn cell disease is also present. Isolated pyramidal tract signs may suggest the somewhat simpler affection, primary lateral sclerosis, a purely descriptive title, and often the first evidence of many diverse disorders affecting the nervous system. Borderline cases cannot be included for analysis.

Seemingly, there could be no dispute as to what constitutes the syndrome of amyotrophic lateral sclerosis. Actually, there is not. Classically, the established disease cannot be mistaken for any other clinical entity. In its pure form it is a student's delight and an instructor's treasure.

Inasmuch as anterior horn cell lesions may occur at any point in the neuroaxis, the manifestations are subject to considerable variation.

There may be a pure bulbar form, but involvement of the upper arm, lower arm, and hand is more common. Cases in which symptoms are confined to the lower extremities are unusual. The cells innervating the bladder and rectum are seemingly unusually resistant. Since the course is often terminated by bulbar nuclear involvement, the higher the level of cellular involvement along the neuroaxis, in general, the shorter the duration of illness. Almost axiomatically it may be said that disease of the pyramidal tract disables, but disease of the anterior horn cell kills.

Fibrillary tremors suggest amyotrophic lateral sclerosis, although they may be found in other diseases associated with chronic irritation of the anterior horn cells, such as syringomyelia, severe neuritides of various types, and intramedullary tumor. When first observed, fibrillary tremor is usually associated with weakness of the implicated muscle; and even may be detected at times by the examiner before muscular weakness becomes evident. Some patients are, peculiarly, very conscious of the muscular twitching, while others, in whom the movements are seemingly extreme, are apparently unaware of them. Frequently the twitching can be palpated better than it can be seen; in fact it may sometimes be felt before becoming visible. This is especially so when weak muscle is covered with a layer of fat. For this reason every weak muscle should be carefully palpated by the examiner before the presence of fibrillary twitching is ruled out. Gross movements of the fingers or slight jerking movements of the forearm on the elbow may result from a fortuitous combination of many twitches. Weakness may not be complained of until obvious atrophy has set in. At this stage shrinking of the intrinsic muscles of the hand with resulting impairment of function, may be conspicious.

Weakness, atrophy and fibrillary tremors are indicative of chronic damage to the anterior horn cells and should always arouse suspicion of amyotrophic lateral sclerosis. If, along with evidence of injury to the anterior

horn cells, very active reflexes are found, the possibility of amyotrophic lateral sclerosis is even more certain. It cannot be stressed too strongly that in the absence of demonstrable sensory changes the occurrence of marked muscular atrophy in the presence of hyperactive reflexes is pathognomonic of amyotrophic lateral sclerosis, and especially so when limited to the upper extremities.

A student's favorite question is the "why" of hyperactive reflexes if there exist signs of disease of the anterior horn cells as well as of the pyramidal tracts. This is easily explained if one remembers that damage is usually confined, within any given segment, to a number of scattered cells, many of the intervening ones retaining their integrity. Any positive influence or "lack of inhibition," capable of producing pyramidal tract signs can, of course, be mediated through the intact cells. If, on the other hand, all of the anterior horn cells supplying a part were damaged, there would be complete paresis and loss of reflexes, as has been observed in one of our cases.

Vitamin E deficiency, in addition to causing damage to the germinal epithelium in male rats, including mesodermal abnormalities in the developing foetus, and producing uterine degeneration with sterility, also may be productive of degenerative changes within the central nervous system. It appears that vitamin E in some fashion is essential to cellular activity.

After experimental studies had shown that vitamin E deficiency was associated with muscular atrophy and paralysis in rats and with specific degenerative effects on the anterior horn cells and the pyramidal tracts, the synthetic form of vitamin E, d,l-alpha-tocopherol acetate* was used by Wechsler[1] in the treatment of amyotrophic lateral sclerosis. Encouraging results were reported in two cases. Bicknell[2] has used the whole wheat germ in cases of amyotrophic lateral sclerosis and other neuromuscular diseases with improvement in almost all cases. Our own experiences are summarized in the following case reports:

Case 1—J. S., age 55, male, was admitted to The Brooklyn Hospital, March 1939, because of difficulty in swallowing and progressive weakness. The onset of the present illness dates back to January 1934 when the lower extremities began to feel weak and the muscles showed signs of early atrophy. By January 1937 the arms had also become weak and stiff. About two years later difficulty in swallowing food and speaking were first noticed.

Physical examination showed generalized muscular atrophy with fibrillary tremors, most marked in the legs. All extremities were severely spastic. Bilateral extensor toe response was obtained. The patient was placed on synthetic vitamin E (Ephynal Acetate) on April 3, 1940. By July 1940 there was a little improvement in physical findings. An increase of weight had occurred and the muscular condition did not seem as stiff as previously. Although no other objective change in the patient's clinical state was noticed at this time, he complained of being weaker, and seemed to be much more restless whenever the medication was withheld.

The patient was seen on November 5, at which time the following notes were recorded. "The patient has deteriorated profoundly since I last saw him. He was completely quadriplegic, the only muscles capable of movement being the sternocleidomastoid and neck muscles and which, nevertheless, were quite weak. There was also paresis of the tongue muscles, with consequent aphonia. Considerable wasting has occurred of all four extremities. Fibrillary tremors which were quite prominent at the last examination had practically disappeared. The disappearance of such tremors in the presence of loss of power would tend to indicate that many of the anterior horn cells were dead. The deep reflexes in the upper extremities were still increased and despite the atrophy the extremities were somewhat contractured and stiff."

It is probable that the patient had not been receiving synthetic vitamin E in adequate dosage for some time. Before changes in the dosage schedule could be made, however, death took place.

In brief, this patient presented a well advanced clinical picture of amyotrophic lateral sclerosis. The signs of bulbar palsy were marked. The course of the illness seems to have been unusually long, beginning with spasticity in the lower extremities and gradually progressing over a period of six years.

* Ephynal Acetate supplied by Hoffmann-La Roche, Inc., Nutley, New Jersey.

Case 2—C. F., age 39, male, was admitted to The Brooklyn Hospital on February 9, 1940 with a complaint of weakness of both arms of three months duration, first noticed while working. Both arms tired easily and cramps occurred on making strenuous movements. Clumsiness in hands and inability to grasp objects were noticed recently. The patient stated that he was less susceptible to cold in cold weather, that the hands seemed warmer than other parts of the body. One month ago slight weakness in the legs on walking became evident.

Physical examination showed slight weakness of the tongue, weakness in use of the hands, and limited adduction and abduction of the fingers. There was atrophy of the intrinsic muscles of both hands. The deep reflexes were hyperactive. An extensor toe response (Babinski) was elicited on the right.

On March 12, 1940 treatment with Ephynal Acetate was begun. Within two months patient stated, "I really believe the medicine has helped me. I can move my legs more freely without getting a gimp or drag in the right leg. I can use my arms without getting a cramp in the muscles. I used to get a very painful cramp in my arms. I feel very good. I feel like doing things and going places. I think I speak better." He had also gained 12 pounds in weight.

About two weeks later he had an acute illness after which there was pronounced weakness of the right hand. By August 9, the patient was able to move the thumb and little finger of right hand a little better. The improvement for a period of four months was definite, at least subjectively. A gain in weight was noted, plus an improvement in a few of the specific complaints, viz. stiffness, cramps, and weakness.

Case 3—S. K., female, was admitted February 8, 1940 to The Brooklyn Hospital. The onset in November 1939 was signaled by a sensation of swelling of the tongue. In one week there was a complaint of "worms crawling up and down the tongue." The tongue also seemed to feel rough and could not be protruded because of weakness. Dysarthria gradually became so marked that the speech was practically unintelligible. Later, the patient had had trouble in swallowing solid food, and there had been much drooling of saliva.

Physical examination revealed a slightly atrophied corrugated tongue with greatly restricted movements, and extensive fibrillary tremors. The bilateral extensor toe sign of Babinski and pathologically active reflexes were found. The vocal cords showed slight dysfunction.

Serologic studies of the blood and cerebrospinal were negative. On February 27, 1940 Ephynal Acetate was given for the first time. By March 26 patient felt stronger, and was doing her own housework.

On May 14, she said she felt stronger and that she was no longer required to lie down in the afternoons because of fatigue. Little objective improvement was detected, however.

About one month after this, because of difficulty in procuring the drug, the patient failed to receive the medication for ten days. During this period she stated that she felt less strong, and could not sleep well. Following reinstitution of therapy, there was again some subjective improvement. Recently there has been a return of weakness of the hands. For five months the patient felt somewhat better, although little objective change was noted.

Case 4—C. B., age 63, female, was admitted April 1940 to The Brooklyn Hospital. In November 1939 the left foot "dragged" and felt heavy, and in December 1939 the right foot also "dragged." The patient began using a cane in January 1940 and walked about up to February 13. There were also complaints of a pain in the back and a feeling of numbness in the legs.

Approximately one year previously (March 1939), she had been sitting in a chair reading when suddenly her leg felt numb. Upon attempting to walk, she fell to the floor. (There seems to be no relationship between this fall and the onset of symptoms eight months later.)

When examined on March 14, 1940 there were signs of bilateral pyramidal tract disease involving both upper and lower extremities. No fibrillary tremors were noted at this time. Later, however, fibrillary tremors were observed in the muscles of the shoulder girdle and tongue. Manometric, cytologic, and chemical studies of the cerebrospinal fluid revealed normal findings.

Vitamin E (Ephynal Acetate) was administered in daily doses of 20 mg. along with

thiamin hydrochloride and liver extract. The daily dose of vitamin B_1 was also 20 mg.

On July 1, 1940 a third examination showed the following: total inability to speak; fibrillary tremors in the tongue; and severe generalized atrophy of the muscles of the shoulder girdle, arms and hands. The legs were spastic and held crossed in the extensor rigidity posture. By July 29, 1940 patient had become absolutely helpless and required the constant attendance of a nurse. Death occurred in February 1941.

In retrospect, the outstanding feature of this case was the development of early spasticity in the lower extremities which progressed to the extremes of extensor rigidity and complete paralysis. The signs of involvement of the anterior horn cells did not appear until later, and then developed rapidly. No improvement occurred following the administration of vitamin E.

Case 5—M. W., age 55, female. In February 1937 some weakness of the left hand was noticed in sewing. The patient could not hold a needle in trying to force it through cloth, and later was unable to hold a pen. The weakness gradually increased throughout the left arm.

When examined February 4, 1938 severe atrophy of the muscles of the left hand and forearm was noted. The left hand was practically useless, only slight movements of the fingers being possible. Weakness of muscles about the shoulder girdle, and also of the elbow was likewise marked. Fibrillary tremors were felt in the deltoid, biceps, triceps and in the muscles of left forearm and also about the left shoulder girdle. Gross twitchings were also evident. A fairly deep layer of fat covered the muscles, so that the fibrillary twitching had to be felt rather than seen. There was a slight right infantile hemiplegia with upper motor neurone signs. The patient was admitted to The Brooklyn Hospital on March 1, 1938 at which time manometric studies of the cerebrospinal fluid revealed normal values.

No further observations were made until April 16, 1940 when evidence of bulbar palsy was found, including atrophy, fibrillary tremors, and weakness of the tongue. The speech was nasal, being barely distinguishable and slight difficulty in swallowing fluids was experienced. The deep reflexes of the lower extremities were definitely hyperactive.

The patient was given vitamin E (Ephynal Acetate), but the medication was not taken regularly. Hence no real estimate of its value could be determined. The right arm was badly paralyzed at this time, and the left was also immobile.

The patient was seen November 11, 1940. A report of her condition then reads as follows: "Patient's condition has advanced steadily to a rather helpless state. Both arms are now virtually paralyzed. The gait is quite spastic. There are obvious manifestations of bulbar weakness, speech being quite unintelligible. At this time the patient coughs badly on attempting to swallow."

Summarizing, the findings in this patient were chiefly those of a flaccid monoplegia of the left upper extremity. The residual right hemiplegia complicated the problem. If the muscles of the left upper extremity had not been palpated, the fibrillary tremors masked by fat would not have been detected. Later the right arm, previously affected by the old infantile hemiplegia became completely paralyzed. The hypotonic state of the musculature as found in this patient's arms is uncommon in this condition. It cannot be said with any positiveness that she received any benefit whatsoever from the use of vitamin E.

Although not suffering from amyotrophic lateral sclerosis, the patient described below was also treated with Ephynal Acetate.

Case 6—H. W., age 62, female, was seen in February 1939. The onset of symptoms occurred in August 1938 with dragging of the left leg. The feeling of weight and stiffness seemed to become progressively worse, making walking very difficult and causing several falls. In January 1939, a feeling of general weakness, together with some stiffness of the right arm was experienced.

Physical examination revealed a spastic paraplegia, the left leg showing an equal degree of involvement despite the absence of complaints relative to it.

Under large doses of vitamin B_1 and liver extract no change occurred. Because of the failure of the patient to improve with this treatment, she was admitted to The Brooklyn Hospital on March 4, 1939. Admission data included Hgb 92%; R.B.C. 4,900,000 and W.B.C. 6,800. On March 7, 1939 an x-ray of cervical spine was taken and found to be

negative.

Subacute combined sclerosis was ruled out by the presence of free hydrochloric acid in the gastric contents. The chief neurological finding was bilateral pyramidal tract signs. There were no physical signs of involvement of the anterior horn cells.

On April 20, 1940 she was placed on vitamin E (Ephynal Acetate) 50 mg. daily, along with vitamin B_1 and nicotinic acid, the latter two drugs being discontinued in the following month. For a long time little improvement could be seen. However, in June, when vitamin E was not available for four days, she remarked, "I did not feel so good."

By July 22, she was able to say, "I am feeling good. I can walk long distances, even on hot days. Legs do not feel heavy."

Discussion

In the five undoubted cases of amyotrophic lateral sclerosis treated with vitamin E, no cures have occurred. One of the patients (Case 5) could not be induced to take the medication regularly so judgement of the value of the drug in this case is not reasonable. The course of the illness in this patient was fairly rapid and uninfluenced by other medications.

Of the remaining four cases, one patient became steadily and rapidly worse despite vitamin E. The other three manifested temporary benefit at least. There was a gain in weight, an increase in the sense of well being and enhanced physical vigor. A lessening of stiffness and loss of cramps in the muscles was evident in one case. A gain in strength, so that housework was performed for a time, was observed in one of these patients. In general, the state of subjective improvement was not maintained, however.

Patient No. 6 at no time showed signs of damage to the anterior horn cells and her illness, therefore, cannot be considered as amyotrophic lateral sclerosis. Definite improvement in this patient's syndrome occurred initially with a combination of nicotinic acid, thiamin hydrochloride, and synthetic vitamin E. Previously, no relief occurred when vitamin B_1 alone had been administered. Whatever improvement resulted in this patient was caused either by nicotinic acid or vitamin E. The former was used for only a brief period, whereas the synthetic vitamin E was taken up to July 22, 1940. This illness, whatever its nature, has been benefited by the use of synthetic vitamin E.

Conclusions

From the observations in the few cases reported, a distinct, but temporary subjective improvement consisting of an increase in vigor and strength, and a gain in weight may be said to have resulted from the use of synthetic vitamin E.

Accordingly, one may conclude that the drug is not without effect in amyotrophic lateral sclerosis. Unfortunately, the improvement in this series has not been maintained. In one case characterized by signs of disease of the pyramidal tracts alone, a definite improvement was observed following the administration of vitamin E, which state of well being has continued to be maintained.

30 Eighth Avenue.

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PSYCHIATRIC THERAPEUSIS IN GENERAL PRACTICE

(Continued from page 309)

The technique of electro-shock is described in the *Texas State Journal of Medicine,* 37: 28, July 1941, and metrazol in *Diseases of the Nervous System,* 1: 10, January 1940. The usage of other specific and special methods of treatment will be described from time to time in the *Diseases of the Nervous System* with the hope that the physician will eventually become his own psychiatrist except perhaps for treatment of the major psychoses. The health of the people will be further improved when this has been accomplished.

T. H. H.

Case Notes in Extramural Psychiatry

Case II. Psychosis With Cerebral Arteriosclerotic Features in a 65-Year-Old White Female

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Complaint Problem—Confusion and fluctuating periods of disorientation associated with ideas of persecution were present. She feels that someone will harm her or take away her money.

Present Illness—The patient was in usual health until Easter, 1940 when she awoke one morning suffering from a bad headache associated with confusion and a "cold." The following night she was said to be "delirious" and since this time has had a deficiency in memory which may be described as "spotty."

A month ago she suffered what was termed another "attack," also characterized by confusion and loss of memory, as well as fear and ideas of persecution about deprivation of money and possessions. She mis-identified her daughter, confusing her with an aunt. This attack gradually cleared up for the most part except for growing fear as night approached and what was termed "nervousness." Two weeks ago she was taken for an auto ride but became confused and fearful. She became so insecure that she insisted that her daughter sleep with her. Sleep was poor. Patient also insisted that a light be kept on in her bedroom. By so doing she feels safer and when she gets up, as is her custom two or three times, she is not so bewildered.

Appetite is poor, there being a loss of some ten pounds since Easter, 1940.

There is occasional constipation for which mineral oil with phenolthaline is exhibited. It is said that she has suffered colitis for the past six years and has been on a special diet. Patient is unduly interested in examining bowel excretions for the purpose of looking for mucous. During the past two years, she has exhibited a growing concentration upon herself.

Patient's 24-hour schedule concerns itself with simple household duties, making beds, washing dishes, assisting in preparing meals, reading the paper, and listening to the radio. She is more devout in prayer and religious observances than the average. She arises earlier than usual in the morning and retires about 10:30 at night. Her daughter sleeps in the same room in a separate bed.

There has been no exhibition of violence or self-destruction. She does, however, get quite irritated with her daughter at times if she is frustrated or an argument ensues about patient's ideas of hearing persons who are intent upon doing her injury, or on occasion ideas of unreality associated with bewilderment as exemplified in the patient's question, "Is this being dead?" Only once did she make a pass at her daughter and that was one night recently. She is inclined to be somewhat accusative, blaming her daughter for kicking her out of bed one night.

Personal History—She is the fourth of six children, of Irish descent. Her birth and early development are normal. Past illnesses have included typhoid fever, broken ribs, and operation for uterine laceration several years ago. It is significant to note that following tonsillectomy several years ago her memory has been more or less impaired.

Personality is described as sweet, lovely, motherly, and a confidant to her friends.

Neurotic traits have been evinced in a life-long fear of lightening and of being alone. This latter has greatly increased during the past year. There has also been present for a long time an obsessive tendency to play with the buttons on her dress in an obsessive fashion. She had a grammar school education, following which she worked in a shirt factory up to the time of marriage. Her husband died nine years after marriage. There

were two offsprings, a son who died in infancy and a daughter, aged 34, single, who takes care of patient.

Patient resides in a large house which is sublet to four men on a rooming house basis.

Family History—Indicates that father died at the age of forty of rheumatic fever. Mother died at the age of eighty of heart disease. Patient has four sisters and one brother, three sisters having died in infancy. It is important to note that a sister aged 67 died three years ago of cerebral hemorrhage after a sickness of six weeks from the time of her first stroke. It is also significant that she died the day after Easter of a second stroke. A brother aged 63 is living, but suffers from stomach and gall stone trouble for which he has had several operations.

There are no nervous or mental illnesses on paternal or maternal side although the latter are characterized by over-concern about money, curiosity, and intense affection for members of their own family and a sort of shrewdness.

Physical Examination — Well-developed, well-nourished female of pyknic habitus; weight 122 pounds; height 5 feet; blood pressure 208/100; pulse 98, regular, good force and volume; peripheral vessels thickened but not tortuous. No adventitious heart sounds; slight enlargement to left.

Cranial Nerves—Smell normal. Wears strong plus glasses, bifocal. Retinal arteries narrow and tortuous; pupils equal, central, and circular; react to light and accommodation; vision subjectively good with glasses; no gross defects in visual fields. III, IV, and VI negative. V negative. VII negative. VIII negative. IX, X, and XI negative. XII negative.

Motor—Muscle tone impaired, general flabbiness but fairly good strength for age. No fibrillations; grips equal; gait normal; no tremor or ataxia; speech normal; no loss of sphincter control.

Sensory—No loss of deep or superficial sensibility. No loss of sense of position or vibratory sense. No tenderness of spine, muscles, or nerves. No pain or hyperesthesia.

Reflexes—Tendon reflexes all active and equal. No clonus. No Hoffmann. Abdominals active, plantars flexor.

Mental Examination—Neat, cooperative, in good social contact. Somewhat on the defensive and mildly suspicious. Frequently smiles in a facetious way, especially to divert attention from memory deficits. Stream of thought connected with respect to responses to inquiries. Tendency to spontaneous irrelevant rambling usually in the direction of a persecutory trend. Objectively in normal mood during examination, although patient has periods of crying associated with morbid introspection of not getting well. Content of thought reveals a persecutory and deprivation trend; fears she will be taken to a hospital and dispossessed of her belongings. At times she confuses her daughter with a dead sister and talks as if the latter were now living. There is also a tendency to reactivate memories about her father and mother. Trend about money concerns itself with the feeling that the daughter may squander what may be left or that someone will take it from her.

Sensorium — Recent memory poor. Only casually concerned with current events. Unable to do seven from one hundred test. Forgetful about utensils on the stove. Will burn toast if not closely supervised. Patient will turn on the hot water and forget to turn it off.

Laboratory Findings—Urinalysis and blood Wassermann negative.

Diagnostic Formulation — Psychosis with cerebral arteriosclerosis associated with senile features and hypertension. Both central and peripheral arteriosclerosis are present. Although there have been no focal symptoms such as paresis and dysarthria, yet the mental picture is essentially one of cerebral arteriosclerosis—spotty memory especially for recent events, two sudden changes (which may be termed "attacks" due to minute capillary cerebral hemorrhage or softening) in behavior associate with memory, judgment, and orientation deficits; fluctuation in mental tension, confusion, especially at night, difficulty in identifying persons at times, but without consistent loss (certain days patient is able to give the correct date), and a tendency to excitement and irritability, especially if crossed by daughter or if visitors touch upon sore spots such as hospitals and money matters. The senile features pertain to facetious manner to smooth over memory deficits, nocturnal prowling with confusion, deficit, especially for recent memory, and tendency to disorientation.

Prognosis—Ultimately poor as condition is progressive. There may be temporary im-

provement coincident with efficacy of cerebral circulation. Focal symptoms are to be expected such as aphasia, hemiplegia, paresis (sensory as well as motor) due to localized cerebral softening or hemorrhage.

Treatment—The most pressing therapeutic need is responsible and trained 24-hour nursing supervisory service in view of the fact of the obvious hazard pertaining to destruction. For example, patient, because of forgetfulness, might neglect to turn off the gas stove or may place inflammable objects in a precarious situation. Matches particularly must be kept out of patient's reach. Erythrol Tetranitrate, ¼ gr. every four hours, was prescribed as well as Elixir Phenobarbital one drachm as required to promote sleep and to allay mental tension. Occupational therapy in the form of simple activities which give comfort such as knitting, crocheting, and simple household duties are to be encouraged. Patient must not be confused in any way. To this end changes in furniture, visiting and other surprise or abrupt modifications should be avoided as she is unable to assimilate rapidly enough for successful adaptation to change. She must be allowed to carry on at her own tempo, avoiding fatigue. There is need for frequent reassurance in view of her threatened ego in the nature of persecutory and deprivation trends. For this reason, a light in the bedroom may be necessary for a while. Her daughter or the nurse sleeping in the same room is likewise indicated for a time. Laxatives as required. Diet: small amounts and frequent if necessary to allay hunger. Avoid roughage and use pureed foods in view of history of colitis. Tea and coffee sparingly. Restriction of salt and fluid intake.

Progress Notes—Within one week blood pressure was reduced to 174/90 and pulse to 88. Patient became more easily reassured and was definitely more comfortable. Suspicious trend prevails, especially toward evening. On certain days there is blueness to the extent of crying, but it lasts a short time. Almost in the next moment she is able to laugh and joke. At times she complains of a sore area at the top of head which she relates to a mild bump while getting into an automobile several months ago. Examination reveals no objective or gross pathology. At no time did patient have headache or tinnitus. Patient finds that a hot drink of milk with a cracker makes for better sleep. Gas on the stomach during the day is relieved by sips of hot tea. There is a reasonable amount of exercise in walking and performing household duties, avoiding any strenuous effort. Judgment is greatly impaired, for example, "I think I know how I got high blood pressure. My collar was too tight." There continues a persecutory trend: "They are saying things about me. I went away—I felt a blue streak. I woke up and didn't know where I was. I cry easily. My throat gets dry."

Patient has continued for three weeks with reduced blood pressure and lower pulse rate until last night when a cousin visited, making for agitation. The next day blood pressure was 216/98 and pulse 96. It became obvious that visitors (at least of an exciting type) must be excluded from the home.

I see no reason why this patient should be hospitalized as long as the family is financially able to maintain adequate 24-hour nursing care at home. Certainly patient and her daughter are much happier with this arrangement.

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A high grade diabetic, dying from generalized carcinomatosis, was observed by one of us (L. K. C.) to require no morphine following a series of convulsions as a result of an insulin reaction of 14 hours' duration. The previous morphine requirement was 4 grains a day. This is in keeping with Sakel's[1] original experience. Since insulin, in doses too small to produce hypoglycemia, is reported to have no effect on drug addiction itself, we attributed the loss of desire for morphine to the convulsions or changes associated with the convulsions. Because of technical difficulties of administering glucose to drug addicts whose veins are usually thrombosed, we chose metrazol as one of the convulsants. In thoroughly searching the medical literature we found no reference to the use of metrazol in the treatment of chronic morphine and heroin addiction.

Metrazol

Patients were hospitalized and given a thorough examination in preparation for metrazol therapy. They were given sufficient morphine sulphate to keep them comfortable and free from withdrawal symptoms. After each convulsion the dose of morphine was reduced by one half, without restriction as to the frequency of administration. At no time during the treatment of these ten patients were there more withdrawal symptoms than they allowed themselves during the time when they practised their addiction. They were placed on high caloric diets. No substitute medication was used to control restlessness. After the complete removal of the drug each patient was placed in isolation for forty-eight hours with the necessary precautions to preclude self-medication.

Of the ten patients treated with metrazol convulsions, eight were women and two were men. Their ages varied from 24 to 40 years. The duration of the addiction ranged from 1½ to 18 years. The daily morphine requirements, to maintain comfort at bed rest, varied from 1¾ to 12 grains. These patients began their addiction with the smoking of opium which was followed with the taking of heroin. In all instances, they administered the drug to themselves by the intravenous route.

It was noted that the morphine medication did not prevent the obtaining of convulsions by usual doses of metrazol. Convulsions were obtained within two hours following ½ grain doses and within three hours of 1 grain doses. In the majority of cases the initial convulsion was obtained with 3.5 to 4 cc. of metrazol. In a few cases it was necessary to use up to 7.5 cc. of metrazol to produce a convulsion. There appeared to be no relationship between the convulsive dose of metrazol and the daily requirement of morphine. Most of the patients had a fear of the metrazol convulsions which became more pronounced as their daily requirement of the morphine was reduced.

Six of the ten cases followed the treatment through to complete withdrawal of the drug. Four refused further treatment after the dose had been reduced to below 1½ grains a day. It was evident to us that these patients were most interested in reducing the monetary outlay necessary to keep themselves comfortable. The time required for the complete withdrawal of morphine depended upon the daily requirements of the patients. Four patients using 3 grains, or less, a day were taken off the drug in five to six days. During this period they received three to four convulsions. Two patients, accustomed to using 6 to 8 grains a day required two weeks for the complete withdrawal of the drug. They were given five to six convulsions. Chart I shows the reduction of daily requirements of mor-

phine sulphate in relation to convulsions in representative patients.

Carbon Dioxide and Oxygen

During the metrazol therapy, one instance was noted in which a convulsive seizure failed to occur, but the metrazol produced a distinct hyperventilation. However, the patient required 3½ grains less morphine in the next 24 hours. Since this reduction was associated with a violent hyperventilation, we decided to use an inhalation of carbon dioxide and oxygen to produce a stimulation of the respiratory center. A mixture of 70 per cent carbon dioxide and 30 per cent oxygen was administered for 60 to 90 seconds by means of a rebreathing apparatus. Such concentrations of carbon dioxide and oxygen produce hyperventilation, short periods of unconsciousness and generalized muscular twitchings. Three patients were treated by this method. Their ages ranged from 21 to 61 years. Their average daily morphine requirements, at bed rest, ranged from 5 to 7 grains. Their periods of addiction ranged from 18 to 40 years. One 60 year old man suffered from mycarditis and chronic bronchitis. A 44 year old man suffered a constriction of the rectum and a woman 39 years of age suffered a bronchiectasis and evidences of hyperthyroidism. Chart II shows the reduction of daily requirements of morphine by this method.

REDUCTION OF DAILY MORPHINE REQUIREMENTS BY CARBON DIOXIDE AND OXYGEN

CHART II

Rebreathing 70 per cent carbon dioxide and 30 per cent oxygen for 60 to 90 seconds.

Days	*R.H*	*C.F.*	*M.O.*
1	4-3/4	5	7
2	*5	*3	*2-1/2
3	*1-1/2	*1-1/2	*2-1/2
4	*1	1-1/2	*1-1/2
5	3/4	1-1/4	1-1/4
6	7/8	1	* 3/4
7	* 3/8	1	3/4
8	0	1	* 1/2
9	0	3/4	1/5
10	0	* 5/8	1/5
11	0	5/8	1/10
12	0	1/2	0
13		X	

REDUCTION OF DAILY MORPHINE REQUIREMENTS BY METRAZOL CONVULSIONS

CHART I

Days	*M.A.*	*J.W.*	*S.R.*	*M.C.*	*F.C.*	*S.M.*	*R.D.*	*M.B.*	*C.S.*	*R.R.*
1	3	2-1/2	1-1/4	7	4-1/2	9-1/2	6-1/2	2	1-3/4	6-1/2
2	*2-1/2	*1-1/2	1	8	6	16	5	*1	2-1/2	8
3	2	*1	* 1/2	*2	*2-1/2	*2-1/2	6	1	* 1/2	*3
4	* 1/2	3/4	3/8	3-3/4	*1-3/4	5-1/2	*3	1	1/2	3-3/4
5	3/4	* 3/8	* 3/8	2	2	*2-1/2	3	1	* 1/16	*1-1/4
6	* 3/4	1/8	0	*1-1/2	1-1/2	3-1/4	*1-3/4	*1	*0	R
7	0	1/8	*0	1-3/4	*1	*1-3/4	2-1/4	1-1/4	0	
8	0	*0	1/8	1-1/4	1-1/4	2	*1-1/4	* 3/4	0	
9			1/8	* 3/4	1-1/4	2	1-1/2	3/4		
10			*0	3/4	* 1/2	2-1/4	1-3/4	*0		
11			0	3/4	1-1/4	2	1	R		
12				1/2	1	*2	1			
13				1/2	* 1/2	1-1/4	R			
14				* 1/4	1/8	1-3/8				
15				1/8	0	R				
16				0	0					

*—Metrazol convulsion. R—Refused to continue treatment.

CHART III

Inhalation of low concentration of carbon dioxide for periods of 1 to 3 hours.

Days	*V.L.*	*F.B.*	*J.W.*	*H.H.*
1	6	2/3	1/2	6
2	3-1/2	2/3	1/2	6
3	5	1/2	1/6	3
4	2-1/2	1/6	1/8	2
5	1	1/6	1/8	2
6	1/2	0	0	2
7	0	0	0	3-1/2
8				R

*—Inhalation of 70 per cent carbon dioxide and 30 per cent oxygen for 60 to 90 seconds.

X—The remaining 1/2 grain withdrawn over 15 days without any treatment.

R—Treatment refused.

While it was possible to obtain the reduction of morphine by using the high carbon dioxide and oxygen mixture, these patients complained even more bitterly of the discomfort of the treatment than did those who were given metrazol. It was also evident that they suffered from greater withdrawal symptoms than those treated with metrazol.

Four patients, who were considered to be in too poor physical condition to justify the use of the methods previously described were given inhalations of low concentration of carbon dioxide. One and one-half to 2 liters a minute were added to the respired air. This mixture was administered in periods of one to three hours, alternating with like periods of rest. Chart III shows the reduction of morphine requirements by this method. Even though there was little discomfort to the breathing of this concentration of carbon dioxide, patients complained very bitterly of the treatment and had more withdrawal symptoms than with the metrazol therapy.

Results

While the methods described allowed for a rather rapid withdrawal of morphine sulphate, very little was accomplished as far as a cure of the addiction. We are fully aware that a cure of addiction implies more than the withdrawal of morphine. We were interested to see if following the administration of metrazol any particular change would occur in the personality of the patient. The follow-up studies on the cases indicates that no such change had occurred. Of the six cases treated by metrazol with complete removal of the drug, five resumed their addiction very shortly. Only one of these five patients remained off morphine for a period of three months. One case was reported to be off morphine at the end of a year.

Of the three cases treated by the administration of 70 per cent carbon dioxide and 30 per cent oxygen, two report freedom from addiction at the end of a year. One is in the federal narcotic penitentiary.

Of the four patients treated with low concentration of carbon dioxide, three completed the withdrawal of the drug. One patient refused to continue after four grains had been withdrawn. Two of the patients have not returned to the addiction. One is reported well at the end of a year. He had been confined to a hospital for nine months following the treatment. The other patient has been off morphine for three months. This patient was not an addict, but morphine was used to control a severe undiagnosed diabetic neuritis. When the morphine was withdrawn and the diabetes brought under control he showed no desire for the drug.

Conclusions

1) The results of the withdrawal of morphine by means of metrazol and the inhalation of carbon dioxide and oxygen are reported in 17 cases.

2) Metrazol convulsions will allow for a rapid reduction of morphine requirements with relative freedom from withdrawal symptoms.

3) Inhalation of carbon dioxide and oxygen allows for the reduction of morphine but does not prevent all withdrawal symptoms.

4) Neither method results in a cure of morphine addiction.

Reference

1 Sakel, Manfred: "Nature and Origin of Hypoglycemia Treatment of Psychosis," *Proceedings of 89th meeting of the Swiss Psychiatric Association at Munsinger*, Berne, May 29, 31, 1937.

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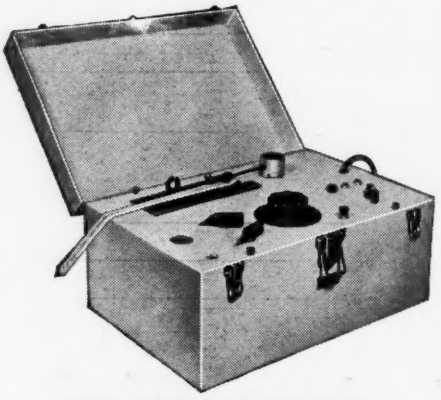

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1 Ebaugh, F. G.: "The Electroencephalogram," Am. J. M. Sc., 196: 882, 1938.

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